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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,142	12/23/2005	Thomas Bar	27097U	5529

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Alexandria, VA 22314

EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
06/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,142	BAR ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-11,13,14 and 16-21* is/are pending in the application.

4a) Of the above claim(s) *9-11,14 and 17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,13 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7, 9-11, 13, 14, 16-17 are pending.

Claims 1-7, 13 and 16 are in applicants elected group I.

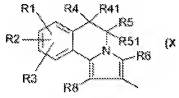
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 03/014116 Bauser et al. WO 03051877 Zhang et al , and WO 0248144 Niewohner et al .

In view of GB1153670, US 4694085, Liebigs Ann. Chwm 9, 1534-1544 1981.(caplus English abstract DN 95:203671.)



Applicants claims are drawn to

And are used as PDE 10 inhibitors.

Scope & Content of Prior Art MPEP 2141.01

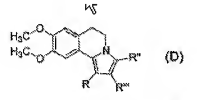
WO 0248144 discloses the compounds see page 1, para 1, claims 1-4, examples 1-91

WO03/014116 discloses similar compounds see page 1, para 2, claim 4 examples 1-92

WO 03051877 page 1, para 1, claims 1-6, examples 1-440.

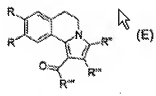
These reference disclose compounds that have been provisoed by the applicants but are very similar and do have the PDE 10 activity.

of GB1153670, US 4694085, Liebigs Ann. Chem 9, 1534-1544 1981 discloses compounds as given on pages 3-5 of WO 03051877.



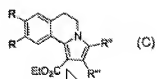
(D)

R = H, CO_2H, CO_2R'''
R'' = H, CO_2H, CO_2R'''
R''' = C_6H_5, CH_3, CO_2R''''



(E)

R = H, CH_3, OCH_3
R'' = H, CH_3
R''' = C_6H_5, CH_3, CO_2R''''
R'''' = H, CH_3



(C)

R = H, OCH_3
R'' = CH_3, C_6H_5
R''' = C_6H_5

These reference do not specify the activity. But they do teach the alkyl at the R6 , and the R8 being a COOR9 , wherein R9 is a H or an alkyl. Thus there is a clear teaching of interchangeability of the substituents.

But the structures has a very close structural similarity.

Difference between Prior Art and the claims MPEP 2141.02

The provisoed compounds have the activity and the compounds of the instant in the GB and US documents do not have the activity.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

One skill in the art would be motivated to modify the compounds of the WO '144, 116, '877 to obtain the compounds of the invention and that of GB '670, US'085 and Liebigs Ann compounds and expect them to have the same activity. Rejections based on structural similarities is founded on the expectations that compounds similar in structure will have similar properties. Note MPEP • 2144.09.

Besides the preamble is not a limitation when the portion of the claim which follows is a self-contained description of a claimed subject matter which does not depend on the preamble for completeness, e.g. where the claim is drawn to a product and the preamble merely recites a property or contemplated use. In re Riden et al (CCPA 1963) 318 F2d 761, 138 USPQ 112; In re Maeder et al (CCPA 1964) 337 F2d 875, 143 USPQ 248.

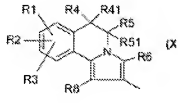
It is noted that the reference does not teach that the composition can be used in the manner instantly claimed, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting. Please note that when applicant claims a composition in terms of function and the composition of the prior art appears to be the same, the Examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection (MPEP 2112).

"The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983).

In re Thuau (CCPA 1943) 135 F2d 344, 57 USPQ 324.

If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPTQ2d 1161, 1165 (Fed. Cir. 1999).

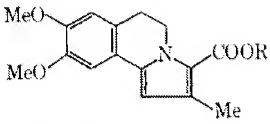
Claim, 1-7, 13 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Casandra et al



Applicants claims are drawn to

Scope & Content of Prior Art MPEP 2141.01

The reference discloses compounds within the scope of applicants compounds.19, 20, 34, 35.



19, R = Et
20, R = H

This reads on applicants compounds when R8 is COOR, R is a H, R1 and R2 are alkoxy, R3, R4, R5, R41, R51 are all H., R6 is a H.

Difference between Prior Art and the claims MPEP 2141.02

The difference is in the position of R6 and R8 and R6 being an alkyl v a Hydrogen.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

One skilled in the art would have found it obvious to exchange R8 and R6. Applicants claims have a preamble which does not carry any patentable weight. The preamble is not a limitation when the portion of the claim which follows is a self-contained description of a claimed subject matter which does not depend on the preamble for completeness, e.g. where the claim is drawn to a product and the preamble merely recites a property or contemplated use. In re Riden et al (CCPA 1963) 318 F2d 761, 138 USPQ 112; In re Maeder et al (CCPA 1964) 337 F2d 875, 143 USPQ 248.

It is noted that the reference does not teach that the composition can be used in the manner instantly claimed, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting.

Please note that when applicant claims a composition in terms of function and the composition of the prior art appears to be the same, the Examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection (MPEP 2112).

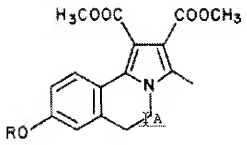
"The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983).

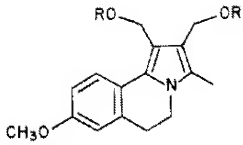
In re Thuau (CCPA 1943) 135 F2d 344, 57 USPQ 324.

If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPTQ2d 1161, 1165 (Fed. Cir. 1999).

Claim 1-7, 11, are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al.

Scope & Content of Prior Art MPEP 2141.01





Difference between Prior Art and the claims MPEP 2141.02

The position of R8 and the methyl group. Are interchanged see compound 7, 8 and 9.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

One of skill in the art would be motivated to modify the compounds as they are just positional isomers. The preamble is not a limitation when the portion of the claim which follows is a self-contained description of a claimed subject matter which does not depend on the preamble for completeness, e.g. where the claim is drawn to a product and the preamble merely recites a property or contemplated use. In re Riden et al (CCPA 1963) 318 F2d 761, 138 USPQ 112; In re Maeder et al (CCPA 1964) 337 F2d 875, 143 USPQ 248.

It is noted that the reference does not teach that the composition can be used in the manner instantly claimed, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural

difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting. Please note that when applicant claims a composition in terms of function and the composition of the prior art appears to be the same, the Examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection (MPEP 2112).

"The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983).

In re Thuau (CCPA 1943) 135 F2d 344, 57 USPQ 324.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 11 and 13 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for substitutents to be H, alkyl, alkoxycarbonylalkyl, cyano, does not reasonably provide enablement for all the various substitutents . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or

use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it.

2) The nature of the invention: The invention is a (highly) substituted compound as PDE 10 inhibitors.

3) The state of the prior art: Synthesizing compounds is very difficult. As given by Dorwald

As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they wereto learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious)

....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the activity as a PDE inhibitors as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group. The method of making theses compounds with numerous functional groups is also very unpredictable as these groups may react with each other and would require an undue amount of experimentation to make these compounds.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are examples to just a limited scope of compounds.

7) The existence of working examples: The instant specification does not have any working examples. On page 46 some compounds with some PDE 10 inhibitory values are given..

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples commensurate to the scope of the claims making and using these requires a high amount of experimentation is burdensome and undue. According to the MPEP even the though some inoperable/enabled embodiments are okay the catch word is "some". Here the majority of compounds are not enabled, making and using them would require an undue amount of experimentation.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Conclusion

Claims 1-7, 11 and 13 stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

June 4, 2009